NTP
National Toxicology Program

NTP Board of Scientific Counselors Technical Reports Review Subcommittee

Report from the December 9, 2004 Meeting

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Toxic Equivalency Factor (TEF) Initiative

- **Dioxin-like compounds are environmental contaminants resulting from a number of sources:**
  - **Combustion**
  - **Chemical manufacturing and processing**
  - **Past production and release**
- **Humans are exposed to mixtures of dioxin-like compounds**
- **Total exposure to mixtures of dioxins is determined by totaling each dioxin's contribution being weighted by its potency relative to the most potent dioxin - 2,3,7,8-TCDD**
- **The World Health Organization Dioxin Toxic Equivalency Factors (TEF'S) are used for this potency adjustment**
- **The validity of the TEF approach for use in cancer risk assessment is uncertain**

Study Objectives

- Test the validity of the TEF method for predicting the carcinogenicity of a simple mixture of dioxins
- Determine the toxicity and carcinogenicity of the individual compounds and mixtures
- Determine potency factors of individual dioxin-like chemicals
- Determine if non-dioxin-like PCBs antagonize the carcinogenicity of a dioxin-like PCB

Chemical	Level of Carcinogenic Activity
	Female Sprague Dawley Rats
PCB-126 and PCB 118	Clear Evidence (Liver, Lung, Oral Cavity)
PCB-153	Equivocal Evidence (Liver)
PCB-126 and PCB 153	Clear Evidence (Liver, Lung, Oral Cavity, Pancreas, Uterus)

Chemical	Level of Carcinogenic Activity	
	Male Mice	Female Mice
3'Azido-3'-thymidine	Clear Evidence (Lung)	No Evidence

Levels of Evidence of Carcinogenic Activity

Chemical	Male Rat	Female Rat	Male Mice	Female Mice
Sodium Chlorate	SE (Thyroid, Pancreas)	SE	NE	EE
Bromodichloromethane	NE	NT	NT	NE
Benzophenone	SE (Kidney)	EE	SE (Liver)	SE (Histiocytic sarcoma)

SE = some evidence

EE = equivocal evidence

NT = not tested

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Anthraquinone (AQ)

- **At the June 29, 2005 meeting the NTP Board requested the Subcommittee revisit reporting of the conclusions of the AQ technical report.**
- **NTP provided additional information on:**
  - **Impurities less than 0.20%**
  - **AQ used in bioassay is not mutagenic in Ames assay**
  - **2-Hydroxyanthraquinone – the major metabolite is several-fold more mutagenic than 9-nitroanthracene, the major contaminant**
- **Subcommittee Actions**
  - **Recommended the title be changed to "Anthraquinone"**
  - **Recommended the first sentence in the conclusions referring to "anthracene-derived" AQ be removed**